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Intrinsic Flexibility of the  $\mu$  Opioid Receptor through Multiscale Modelling Approaches - COMP403

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## 403 - Intrinsic flexibility of the $\mu$ opioid receptor through multiscale modeling approaches

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### Abstract

Recent releases of numerous G protein-coupled receptors crystalline structures created the opportunity for computational methods to widely explore their dynamics. Here, we study the biological implication of the intrinsic flexibility properties of  $\mu$  opioid receptor ( $\mu$ OR). First, one performed classical all-atom (AA) Molecular Dynamics (MD) simulations of  $\mu$ OR in its apo-form. We highlighted that the various degrees of bendability of the  $\sigma$ -helices present important consequences on the plasticity of the  $\mu$ OR binding site. Hence, this latter adopts a wide diversity of shape and volume, explaining why  $\mu$ OR interacts with very diverse ligands. Then, one introduces a new strategy for parameterizing purely mechanical but precise coarse-grained (CG) elastic network models (ENMs). Those CG ENMs reproduced in a high accurate way the flexibility properties of  $\mu$ OR as observed with the AA simulations. At last, ones uses network modularization to design multi-grained (MG) models. They represent a novel type of low resolution models, different in nature *versus* CG models as being true multi-resolution models, *i.e.*, each MG grouping a different number of residues. The three parts of our work constitute an integrated hierarchical and multiscale approach for tackling the flexibility of  $\mu$ OR.

Time	Wednesday, March 21, 2018 4:15 PM
Session	COMP: Structure-Based Drug Design for GPCRs: PM session (1:30 PM - 4:50 PM)
Location	New Orleans Marriott Convention Center
Room	Blaine Kern F